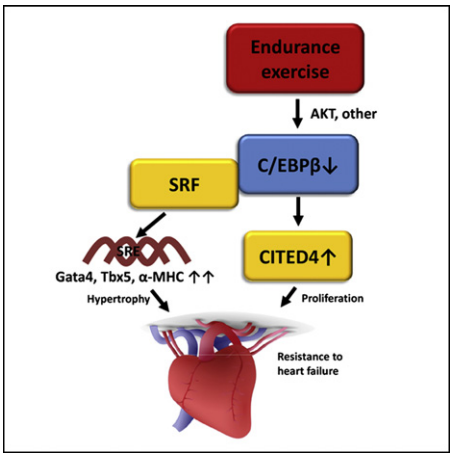
# In This Issue

Cell




## Cardio Workout, No Sweat

PAGE 1072

The human heart grows in response to exercise, but mechanisms that drive this remodeling are still mysterious. Now Bostrom et al. find that endurance exercise triggers a proliferative program in cardiomyocytes that depends on reduced expression of the transcription factor C/EBPβ and upregulation of the CREB-binding protein CITED4. Importantly, genetic manipulation of this pathway mimics the exercise state and protects the heart from pathological insults.

## Stem Cell Origins for Duchenne Muscular Dystrophy

PAGE 1059

Mutations in the *dystrophin* gene cause Duchenne muscular dystrophy (DMD) in humans, but the same defect in mice yields a surprisingly mild phenotype. Now, Sacco et al. generate a mouse model of DMD that closely resembles the human disease and, in the process, find that loss of muscle stem cells (MuSC) contributes to DMD. Mice lacking both telomerase activity and the *dystrophin* gene exhibit defects in MuSCs proliferation and regeneration of damaged muscles, suggesting that DMD is ultimately a stem cell disease.

## The Food of Our Fathers

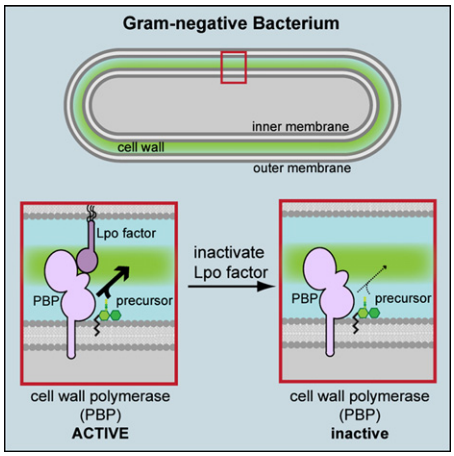
PAGE 1084

In this issue, Carone et al. demonstrate that fathers can transmit environmental information to their offspring. Male mice fed a low-protein diet father offspring with altered lipid metabolism and gene expression compared to offspring of fathers fed a normal diet. These changes correspond to cytosine methylation differences in a putative PPARγ enhancer in the offsprings' livers. Thus, environmentally induced paternal effects can transfer to the next generation even without interactions between parent and child.

## Building a Wall from Both Sides

PAGE 1097 and PAGE 1110

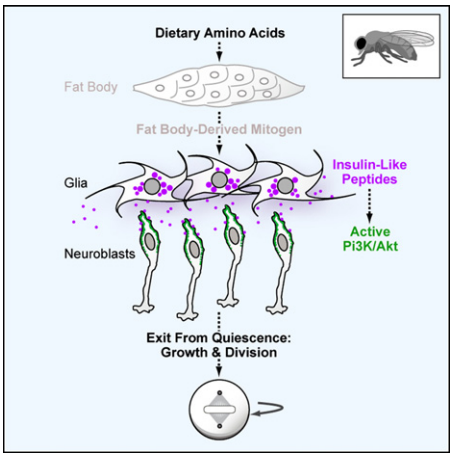
Building a bacterial cell wall obviously requires infrastructure and input from the cytosol. Now, two groups, Typas et al. and Pardis-Bleau et al., report that outer-membrane components are also critical for constructing this peptidoglycan-rich layer. Both groups identify two outer-membrane lipoproteins in *E. coli* that are required for activating penicillin-binding proteins, the enzymes that synthesize peptidoglycan and the targets of penicillin. These results suggest that cell wall biogenesis in bacteria is a coordinated effort by components in both the inner and outer cell membranes.




## PolyQs Are Curly Qs

PAGE 1121

At least ten neurodegenerative diseases, including Huntington's disease, are associated with the aggregation of proteins enriched in glutamine/asparagines residues (Q/N-rich) or with expanded glutamine repeats (polyQ). In contrast to the current view that these proteins misfold into β sheet-rich structures, Fiumara et al. find that amino acid sequences of polyQ and Q/N-rich proteins, as well as their interactors, display features of α-helical coiled coils. Moreover, structure-guided mutagenesis demonstrates that coiled-coil stability regulates aggregation and cellular toxicity of polyQ proteins and prion activity of Q/N-rich proteins.




## Glia Give Neuroblasts a Wake-Up Call

PAGE 1161

To maintain and repair tissue, stem cells must reawaken from a quiescent state and resume proliferation. Chell and Brand now show that glial cells reactivate neighboring neural stem cells in the *Drosophila* CNS. In response to a nutrient stimulus, glial cells express insulin-like peptides that kick-start the insulin/PI3K pathway in nearby stem cells, activating their growth and proliferation. These results demonstrate that targeting support cells may represent an effective strategy for manipulating stem cell behavior.

## The Inhibitor Wnt into the MVB

PAGE 1136

For Wnt signaling to occur, the kinase GSK3 must be blocked. In this issue, Taelman et al. report that, instead of directly inactivating GSK3, Wnt signaling takes a more stealthy approach. It sequesters GSK3 inside membrane-bound organelles derived from multivesicular bodies (MVBs), which normally traffic cell surface receptors to late endosomes. Sequestration of GSK3 extends the half-life of numerous GSK3 substrates, including β-catenin, indicating that MVBs are a critical component of canonical Wnt signaling.

## Meningitis Breaks the Endothelial Barrier

PAGE 1149

Meningococcus, the cause of cerebrospinal meningitis, gains access across the blood-brain barrier by interacting with an unknown host receptor. Now, Coureuil et al. report that proteins on bacterial pili open anatomical gaps in endothelial cells by stimulating a β2-adrenoceptor β-arrestin signaling pathway in the host. This triggers the relocalization of cytoskeletal and junctional proteins from tight junctions to the site of extracellular bacterial colonies, leading to the stabilization of bacterial adhesions and disruption of endothelial integrity.

## Constellation of Tissue-Specific Phosphorylation

PAGE 1174

Huttlin et al. chart the scope of tissue-specific gene expression and intracellular signaling by presenting comprehensive proteomic and phosphoproteomic analyses for nine different mouse tissues. Their data uncover >36,000 phosphorylation sites with >50% new sites and indicate that phosphorylation is independent of protein abundance. Although most phosphoproteins are widely expressed across multiple tissues, they often display tissue-specific phosphorylation that tunes their activity to the particular needs of each tissue.